DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/17/10 has been entered.

2. Claims 18, 20, 21 and 29-45 are pending.

Claims 18, 20 and 21 stand withdrawn from further consideration by the examiner under 37 CFR 1.142 (b) as being drawn to a nonelected invention. Therefore, claims 29-45 are currently being examined.

3. Applicants' IDS filed on 9/17/10 has been acknowledged.

4. In light of Applicant's amendments filed on 9/17/10, the rejections set forth in the office action mailed on 5/19/10 (see sections 5-9) have been withdrawn. The claim amendment filed on 9/17/10 cancels claims 1-17 and 22-28. The following rejection remains.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 29-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,171,586 (IDS reference filed on 5/16/06, of record) in view of U.S. Pub. 2005/0142139A1(of record) for the reasons set forth in the office action mailed on 5/19/10.

The '586 patent teaches a stable aqueous pharmaceutical formulation comprising a buffer at about pH 4.8 and the antibody encompasses polyclonal antibody (col. 7-8, claims 1-29). Note that the '586 patent includes polyclonal antibody in the antibody (col. 7).

Given that the '586 patent does not disclose nicotinamide, the claimed limitation "wherein the preparation does not comprise nicotinamide" has been met.

The disclosure of the '586 patent differs from the claimed invention in that it does not teach the use of proline as is currently recited in claim 29 of the instant application.

The '139 publication teaches CD4-IgG2 antibody formulation comprising a histidine buffer and proline at about pH 5.5 (claims 29-39, [0032]). Given that the specification on p.4 of the instant application discloses that all naturally occurring amino acid is L-amino acid and the '139 publication discloses naturally occurring amino acids, it meets the limitations of claims 33-36 of the instant application.

As the '139 publication does not disclose any use of nicotinamide as a stabilizer, the referenced formulation is considered to be made in the absence of nicotinamide. Thus, meets the claimed limitation of claim 29.

Further, the '139 publication teaches that the concentration of the antibody is 15-162mg/ml ([0045-47]) and proline concentration of "about" 25-150mM ([0013]).

Note the term "about" is flexible and includes unrecited limitations near the recited limitation. Given that the '139 publication teaches the proline concentration of "about"150mM and reads on claimed limitation of "at least 0.2M" or "0.2M", claims 7 and 8 are included in this rejection.

As is evidenced by the specification on p. 6 of the instant application, 10% of IgG is equivalent to 100g/L. Given that the concentration of 100g/L is equivalent to 100mg/ml, the referenced about 100-162mg/ml that are suitable for subcutaneous or IV are equivalent to 10-16.2% (w/v) ([0007, 0049]) and claims 10-13 are included in this rejection.

Moreover, the referenced histidine buffer is considered as "pharmaceutically acceptable additives", claims 16 and 23 are included in this rejection. Further, claims 34, 36 and 40 reciting "wherein the preparation is a liquid preparation that has not been subject to lyophilization" are included in this rejection because the '139 publication specifically recites "stable following at least one freeze and thawing of formulation" (claim 16) which differentiate the physical condition of the formulation from recited "lyophilized"(claim 15) which is subject to lyophilization. Therefore, the reference teachings anticipate the claimed invention.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add proline as a stabilizer as taught by the '139 publication to the antibody formulation as taught by the '586 patent.

Therefore, it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of proline improves stability of protein upon storage and delivery by reducing aggregation.

From the teachings of the references, it would have been obvious to one of ordinary skill in the art to combine teachings of the references and there would have been a reasonable expectation to success in producing the claimed invention. Therefore, the invention as a whole was a prima facie obvious to one of ordinary skill in the art at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 9/17/10 have been fully considered but they were not persuasive.

Applicant has traversed the rejection based on that the combination of the references is not obvious. Applicant has asserted that the prior art references do not apply to polyclonal IgG preparation, the prior art does not discloses the claimed pH range as well as other stabilizes in addition to proline. Thus, the combination of the references does not result in the claimed invention. Moreover, the claimed invention shows unexpected results and commercial success and the evidence of secondary consideration overcomes the obviousness.

Contrary to Applicant's assertion, the '586 patent clearly defines the polyclonal antibody included in the "antibody" (note col. 7) and the '139 publication teaches the use of proline. One cannot show nonobviousness by attacking references individually where the rejection is based on combination of the references. See MPEP 2145.

Further, contrary to Applicant's assertion, the prior art pH range is between about pH 4.8 and pH 5.4. Given that the term "about" considers flexible, the term about includes pH near pH 4.8 and pH 5.4. Regardless, the claimed pH 5.4 is included in the prior art pH ranges.

With respect to Applicant's assertion of secondary consideration and addition of other stabilizers, these assertions have not been found persuasive. Applicant has asserted that the histidine, other stabilizers or other amino acids are not required in the claimed preparation. Applicant's assertion of the secondary considerations is substantiated by the excerpts from FDA and the Cramer article.

However, the secondary consideration is not sufficient to obviate the evidence of obviousness and the scope of the claimed invention is not commensurate with the references submitted by Applicant.

Note that the excerpt discloses that the formulation consisting of proline and antibody can be stored at room temperature for 2-3 years while the claimed formulation comprising a proline and antibody. The term comprising is considered open and it allows addition of other unrecited stabilizers and amino acids in addition to proline. Further, the independent claim 29 does not need to be in the aqueous form or as in the room temperature for 2-3 years as applicant has asserted. Applicant argues the limitations that are not recited in the claims. Applicant is advised to amend the claims accordingly if Applicant intends to claim such properties as unexpected results. Therefore, the combination of the references remains obvious and the rejection is maintained.

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F, 9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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